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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,191	12/10/2001	William Gaarde	RTS-0274	8633

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FENWICK & WEST LLP
801 CALIFORNIA STREET
MOUNTAIN VIEW, CA 94014

EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,191	GAARDE ET AL.	
	Examiner	Art Unit	
	Sean R McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-14* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/10/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I and SEQ ID NO: 48 in Papers filed 3/04/04 is acknowledged. It is noted that upon examination and search of SEQ ID NO:48, it became apparent that the search of SEQ ID NOS: 47, 63, and 64 would not be a burden in addition to SEQ ID NO: 48. SEQ ID NOS: 47, 48, 63 and 64 have been examined.

Claims 15-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Papers filed 3/04/04.

It is noted that claim 11 should have been indicated as a linking claim in the restriction mailed 2/5/04. Claim 11 is examined as a linking claim in the instant Official Action.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Dunn et al (Accesssion No. AZ781130 an Database rst.seq, 16 February 2001).

Dunn et al disclose a 25mer oligonucleotide that corresponds to nucleotides 1793-1817 of SEQ ID NO: 19. The oligonucleotide therefore contains all the required

structural elements recited in the claims. The function recited in the claims is assumed to be possessed by the disclosed oligonucleotide of Dunn without evidence to the contrary.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al [Accession No. R06912 on Database rst.seq, 05 April 1995].

Hillier et al disclose an oligonucleotide that corresponds withnucleotides 2008-2044 of SEQ ID NO: 19. The oligonucleotide therefore contains all the required structural elements recited in the claims. The function recited in the claims is assumed to be possessed by the disclosed oligonucleotide of Hillier et al without evidence to the contrary.

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Schmidt et al [US 6,358,741].

See column 18 where several antisense oligonucleotides targeted to inhibit CTGF are disclosed.

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Hishikawa et al [European Journal of Pharmacology, cited by applicant].

Hishikawa et al have disclosed an antisense targeted to inhibit CTGF expression, see page 287, for example.

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Shimo et al [cited by applicant].

Shimo et al have disclosed an antisense oligonucleotide for inhibition of CTGF expression, see page 132, for example.

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Hishikawa et al [The Journal of Biological Chem., cited by applicant].

Hishikawa et al have disclosed antisense oligonucleotide to inhibit CTGF expression, see page 37462, for example.

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4-10 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al [US 6,358,741], Hishikawa et al [European Journal of Pharmacology, cited by applicant], Kubota et al [cited by applicant], El-Din et al [cited by applicant],Shimo et al [cited by applicant], Hishikawa et al [The Journal of Biological Chem., cited by applicant], Baracchini et al [US 5,801,154], and Bennett et al. [US 5,998,148].

The claimed invention is drawn to antisense oligonucleotides hybridizable to the 3' UTR of a nucleic acid encoding connective tissue growth factor (SEQ ID NO: 19). The oligonucleotides are 8-50 nucleobases in length can have sugar, base, and backbone modifications as recited in the claims and can be part of compositions that include the oligonucleotide and carriers as recited in the claims.

Schmidt et al have taught to target CTGF with antisense oligonucleotides such as phosphorothiates, lengths of 15-100 nucleotides. It has been taught that antisense oligonucleotides can have modified bases, backbone linkages. It has been taught that one can look to orthologs to design antisense, for example. It has also been taught tto include antisense oligonucleotides in pharmaceutically acceptable carriers. See columns 16-20 and Example 2.

Hishikawa et al have disclosed antisense oligonucleotides to inhibit CTGF expression and disclose CTGF s association with vascular disease.

Kubota et al have taught the inhibition of CTGF via an antisense 3'UTR construct.

El-Din et al have taught that CTGF is a target for therapeutic intervention in fibrotic disease and have taught the inhibition of CTGF via antisense oligonucleotides, see pages 281 and 284, for example.

Shimo et al have taught the inhibition of CTGF via antisense targeted to CTGF and have taught the association of CTGF an vascular disease, for example.

Hishikawa et al have taught the association of CTGF expression and various diseases and have taught the inhibition of CTGF via antisense oligonucleotides.

The prior arthas therefor taughtantisense of the recited length, modifications to antisense oligonucleotides , pharmaceutical carriers, etc. the prior art does not specifically teach targeteing the 3'UTR of a nucleic acid SEQ ID NO: 19. It is noted that SEQ ID NO: 19 was known at the time of invention as evidenced at page 91 of the specification. The art cited above in combination with the teachins below clearly show the claimed invention to be obvious.

Bennett et al have taught general targeting guidelines at columns 3-4, for example. It has been taught to target 5'untranslated regions, start codons, coding regions, and 3'untranslated regions of a desired target, for example. It has been taught in column 5, for example, that antisense compounds are commonly used as research reagents and diagnostics, for example. At column 5 it has been taught that antisense

oligonucleotides 8-30 nucleotides in length are particularly preferred. At columns 6-7 it has been taught preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, for example. At columns 7-8 it has been taught that preferred antisense oligonucleotides comprise modified sugar moieties including2'-O-methoxyethyl. It has also been taught to modify nucleobases in antisense oligonucleotides at column 8-9 which includes the teaching of 5-methyl cytosine and at column 10 it has been taught chimeric antisense oligonucleotides. All of the above referred to modification are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. At columns 10-24, for example it has been taught numerous "carriers" for antisense oligonucleotides. In table I it has been taught the successful targeting of those regions taught in columns 3-4 with chimeric phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification).

Baracchini et al have taught, at column 6 for example, that antisense oligonucleotides can be used for research purposes and have also taught at column 6 that antisense oligonucleotides can be modified in their sugars, backbone linkages and nucleobases and that such modifications are desirable in antisense since these modifications have desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid targets and increases stability in the presence of nucleases. Baracchini et al provide specific examples of such modifications at columns 6-8 and in Example 1, for example. These specific examples taught by Baracchini et al include phosphorothioate linkages, 2'-O-methoxyethyl sugars, 5-methylcytosine and

chimeric oligonucleotides, for example. It has been taught to target 5'untranslated regions, start codons, coding regions, and 3'untranslated regions of a desired target, for example.Tables 1-4 show the successful design and use of modified oligonucleotides in cells in culture, for example. Table I therefore reflects the successful practice of general antisense design taught at columns 8-10, for example. At column 4 it has been taught various carriers for antisense delivery. It has been taught at column 8 that antisense are preferably 8 to 30 nucleotides and that it is more preferable to make antisense oligonucleotides that are 12 to 25 nucleotides in length, for example.

The prior art has therefore taught all aspects of the claimed invention. The prior art has shown clearly a motivation to inhibit CTGF via antisense oligonucleotides and the prior art has shown all of the recited limitations as known modifications and carriers used in antisense design. It has also been shown to use a 3'UTR antisense to inhibit CTGF and it has been taught be the art to target a 3'UTR of a desired target, for example.

The invention as a whole would therefore have been prima facie obvious to one in the art at the time the invention was made.

Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting nonelected subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SRM

SEAN McGARRY
PRIMARY EXAMINER
1635